

REMARKS

Claims 1-34 are pending, claims 9-15 and 29-34 are withdrawn from consideration. Applicants incorporate by reference the Response and Amendment filed on July 14, 2003.

Rejection of Claims 1-6, 8, 16, 18-21, 23, 24, 27 and 28 under 35 U.S.C. § 103(a)

Claims 1-6, 8, 16, 18- 1, 23, 24, 27 and 28 were rejected under 35 U.S.C. §103(a) as being unpatentable over Patterson et al. (Electrophoresis 17: 877-891 (1996)) in view of Formosa et al. (Methods in Enzymology 208: 24-45 (1991)). The Office Action states that:

Applicant argues that Formosa et al does not teach or suggest that the use of two or more columns with varying ligand concentrations would be useful for isolation and/or identification of an interacting protein. This is not found persuasive because Examiner has not relied upon Formosa for teaching the identification of an interacting protein but rather has relied upon Patterson for this teaching. Further, Formosa et al teaches the characterization of interacting proteins and therefore is considered to be analogous art.

The rejection is respectfully traversed.

Obviousness can only be established by combining or modifying the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art (see MPEP 2143.01). Furthermore, the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination (see MPEP 2143.01 citing *In re Mills*, 916 F.2d 680 (Fed. Cir. 1990)). Applicants respectfully assert that the Examiner has failed to provide a motivation to combine the disclosure of Patterson et al. with the disclosure of Formosa et al.

Patterson et al. is relied on for disclosing affinity chromatography whereby the eluted proteins are subjected to gel electrophoresis and mass spectrometry. Patterson et al. uses a single concentration of immobilized ligand and identifies three proteins that interact with the protein immobilized on the column. Clearly someone reading Patterson would not be motivated to conduct an affinity chromatography experiment *using two or more columns* with varied concentrations of ligand, as presently claimed, when Patterson et al. discloses use of just *a single column* at a single ligand concentration.

As stated in the Response filed on July 14, 2003, Formosa et al. discloses that identification of an optimum concentration of ligand is essential. Furthermore, Formosa et al. discloses that concentrations of ligand that deviate from the optimum concentration may have negative effects. For example, ligand concentrations that are too low may result in failure to obtain adequate amounts of the interacting protein and ligand concentrations that are too high may result in significant nonspecific binding. Accordingly, one of ordinary skill in the art would not be motivated to isolate and/or identify an interacting protein using two or more columns with *varying concentrations of ligand*, as presently claimed, based on the disclosure of Formosa et al., because Formosa et al. discloses that an optimal ligand concentration is essential for such purposes and that ligand concentrations which are too high or too low should not be used.

A combination of Patterson et al. with Formosa et al. would actually seem to teach away from the embodiment presently claimed that uses two or more columns with varying concentrations of ligand for isolating and/or identifying an interacting protein. Patterson et al. discloses that a single column may be used to identify interacting proteins and Formosa et al. discloses that identification of *an* optimum ligand concentration is essential for affinity chromatography experiments. Therefore, the combination of the two references would indicate that affinity chromatography experiments *should be carried out on a single column with an optimal ligand concentration*. There is no motivation to combine the disclosure of Patterson et al. with the disclosure of Formosa et al. Furthermore, even if those disclosures were combined, neither reference either alone or in combination, teach or suggest each and every element of the embodiment presently claimed. Accordingly, the cited references, either alone or in combination, fail to teach or suggest the currently claimed embodiments.

The Examiner further alleges that Formosa et al. "shows that RAP38 eluted from the column varies proportionately with the concentration of immobilized ligand" and points to lane a (0 μ g of immobilized protein) as compared to lane b (20 μ g of immobilized protein) of Figure 1A. Contrary to the Examiner's assertions, Applicant's respectfully submit that Figure 1A does not clearly indicate that the concentration of eluted protein varies proportionately with the concentration of ligand immobilized on the column. For example, lanes g (0 μ g immobilized protein) and h (10 μ g immobilized protein) appear to show approximately the same amount of RAP38 eluting from the column. Furthermore, lane i (0 μ g of immobilized protein) appears to

show more RAP38 eluting from the column than lane j (2 µg of immobilized protein).

Accordingly, this figure taken as a whole fails to clearly teach or suggest that the amount of interacting protein eluting from the column varies proportionately with the concentration of immobilized protein ligand.

Applicants respectfully remind the Examiner that the references must be viewed as a whole and must suggest the desirability of the claimed invention without the benefit of impermissible hindsight reconstruction afforded by the claimed invention. Furthermore, in order “[t]o establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art.” MPEP §2143.03 citing *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Neither Patterson et al. nor Formosa et al., either alone or in combination, teach or suggest each and every element of the embodiment presently claimed. Accordingly, the cited references, either alone or in combination, fail to teach or suggest the currently claimed embodiments. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of Claims 7, 17, 22, 25 and 26 under 35 U.S.C. § 103(a)

Claims 7, 17, 22, 25 and 26 were rejected under 35 U.S.C. §103(a) as being unpatentable over Patterson et al. in view of Formosa et al. as applied to claims 1-6, 8, 16, 18-21, 23, 24, 27 and 28 above, and further in view of Vestal et al (US 6,281,493).

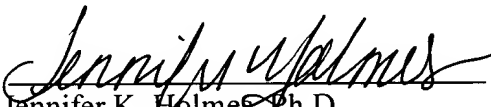
As discussed above, Patterson et al. in view of Formosa et al. fail to teach or suggest the currently claimed embodiment. Further, Applicants respectfully submit that Vestal et al. fail to make up for the deficiencies of Patterson et al. and Formosa et al. In particular, Vestal et al. fails to teach or suggest a method for identification of an interacting protein using affinity chromatography on two or more columns having varying concentrations of an immobilized protein ligand and wherein the amount of said interacting protein eluting from the columns varies proportionately with the concentration of immobilized protein ligand, as presently claimed. Accordingly, the cited references, either alone or in combination, fail to teach or suggest the currently claimed embodiments. Reconsideration and withdrawal of the rejection is respectfully requested.

Applicants believe that the claim amendments and remarks made herein fully address all issues raised in the Office Action. Silence with regard to any of the Examiner's rejections is not an acquiescence to such rejections. Specifically, silence with regard to Examiner's rejection of a dependent claim, when such claim depends from an independent claim that Applicant considers allowable for reasons provided herein, is not an acquiescence to such rejection of the dependent claim(s), but rather a recognition by Applicant that such previously lodged rejection is moot based on Applicant remarks and/or amendments relative to the independent claim (that Applicant considers allowable) from which the dependent claim(s) depends.

CONCLUSION

Applicants consider the Response herein to be fully responsive to the referenced Office Action. Based on the above Remarks, it is respectfully submitted that this application is in condition for allowance. Accordingly, allowance of the pending claims is requested. If a telephone conversation with Applicants' Agent would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 832-1000.

Respectfully submitted,

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